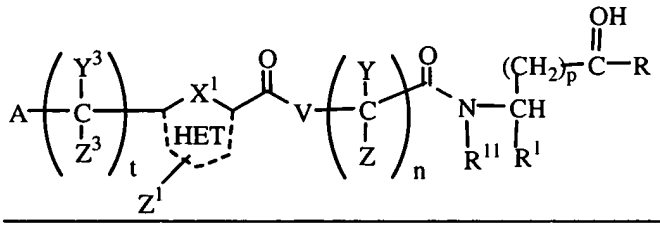
III. Amendments to the Claims

Cancel claims 1-12. Please amend claims 13-22 as follows:

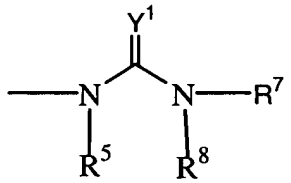
Claims 1-12 (Cancelled)

Claim 13 (Currently Amended) A method for treating conditions mediated by the $\alpha_v\beta_3$ integrin in a mammal in need of such treatment comprising administering a therapeutically effective $\alpha_v\beta_3$ inhibiting amount of a compound ~~according to Claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 11~~ of Formula I:



or a pharmaceutically acceptable salt thereof, wherein

HET is a 5-8 membered monocyclic heterocyclic ring, optionally unsaturated, containing 1 to 4 heteroatoms, selected from the group consisting of O, N, or S, wherein X^1 is selected from the group consisting of CH, CH_2, N, NH, O and S;

A is 

wherein Y^1 is selected from the group consisting of N—R^2, O, and S;

R^2 is selected from the group consisting of H; alkyl; aryl; hydroxy; alkoxy; cyano; nitro; amino; alkenyl; alkynyl; amido; alkylcarbonyl; arylcarbonyl; alkoxycarbonyl; aryloxycarbonyl; haloalkylcarbonyl; haloalkoxycarbonyl; alkylthiocarbonyl; arylthiocarbonyl; acyloxymethoxycarbonyl; alkyl optionally substituted with one or more substitutent selected from lower alkyl, halogen,

hydroxyl, haloalkyl, cyano, nitro, carboxyl, amino, alkoxy, aryl or aryl optionally substituted with one or more halogen, haloalkyl, lower alkyl, alkoxy, cyano, alkylsulfonyl, alkylthio, nitro, carboxyl, amino, hydroxyl, sulfonic acid, sulfonamide, aryl, fused aryl, monocyclic heterocycles, or fused monocyclic heterocycles; aryl optionally substituted with one or more substituent selected from halogen, haloalkyl, hydroxy, lower alkyl, alkoxy, methylenedioxy, ethylenedioxy, cyano, nitro, alkylthio, alkylsulfonyl, sulfonic acid, sulfonamide, carboxyl derivatives, amino, aryl, fused aryl, monocyclic heterocycles and fused monocyclic heterocycle; monocyclic heterocycles; and moncyclic heterocycles optionally substituted with one or more substitutent selected from halogen, haloalkyl, lower alkyl, alkoxy, amino, nitro, hydroxy, carboxyl derivatives, cyano, alkylthio, alkylsulfonyl, sulfonic acid, sulfonamide, aryl or fused aryl; or

R^2 taken together with R^7 forms a 4-12 membered dinitrogen containing heterocycle optionally substituted with one or more substituent selected from the group consisting of lower alkyl, thioalkyl, alkylamino, hydroxy, keto, alkoxy, halo, phenyl, amino, carboxyl or carboxyl ester, spirodioxolane, and fused phenyl; or

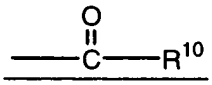
R^2 taken together with R^7 forms a 4-12 membered heterocycle, optionally unsaturated, containing one or more heteroatom selected from O, N and S; or

R^2 taken together with R^7 forms a 5-9 membered heteroaromatic ring optionally substituted with one or more substituent selected from lower alkyl, phenyl, alkoxy and hydroxy;

R^2 taken together with R^7 forms a 5 membered heteroaromatic ring fused with a aryl or heteroaryl ring;

R^7 (when not taken together with R^2) and R^8 are independently selected from the group consisting of H; alkyl; alkenyl; alkynyl; aralkyl; amino; alkylamino; hydroxy; alkoxy; arylamino; amido; alkylcarbonyl; arylcarbonyl; haloalkoxycarbonyl; alkylthiocarbonyl; arylthiocarbonyl; acyloxymethoxycarbonyl; cycloalkyl; bicycloalkyl; aryl; acyl; benzoyl; alkyl optionally substituted with one or more substiuent selected from lower alkyl, halogen, hydroxy, haloalkyl, cyano, nitro, carboxyl derivatives, amino, alkoxy, thio, alkylthio, sulfonyl, aryl, aralkyl, aryl optionally substituted with one or more substituent selected from halogen, haloalkyl, lower alkyl, alkoxy, methylenedioxy, ethylenedioxy, alkylthio, haloalkylthio, thio, hydroxy, cyano, nitro, carboxyl derivatives, aryloxy, amido, acylamino, amino, alkylamino, dialkylamino, trifluoroalkoxy, trifluoromethyl, sulfonyl, alkylsulfonyl, haloalkylsulfonyl, sulfonic acid, sulfonamide, aryl, fused aryl, moncyclic heterocycles or fused moncyclic heterocycles; [monocyclic heterocycles;] monocyclic heterocycles optionally substituted with one or more substitutent selected from halogen, haloalkyl, lower alkyl, alkoxy, aryloxy, amino, nitro, hydroxy, carboxyl derivatives, cyano, alkylthio, alkylsulfonyl, aryl, fused aryl; monocyclic and

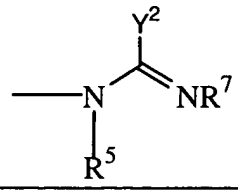
bicyclic heterocyclicalkyls; $-SO_2R^{10}-$ wherein R^{10} is selected from the group consisting of alkyl, aryl and monocyclic heterocycles, all optionally substituted with one or more substituent selected from the group consisting of halogen, haloalkyl, alkyl, alkoxy, cyano, nitro, amino, acylamino, trifluoroalkyl, amido, alkylaminosulfonyl, alkylsufonyl, alkylsulfonylamino, alkylamino, dialkylamino, trifluoromethylthio, trifluoroalkoxy, trifluoromethylsulfonyl, aryl, aryloxy, thio, alkylthio, and monocyclic heterocycles; and



wherein R^{10} is defined above; or

NR^7 and R^8 taken together form a 4-12 membered mononitrogen containing moncyclic or bicyclic ring optionally substituted with one or more substitutent selected from lower alkyl, carboxyl derivatives, aryl or hydroxy and wherein said ring optionally contains a heteroatom selected from the group consisting of O, N, and S;

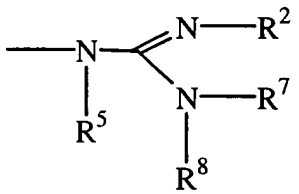
R^5 is selected from the group consisting of H, alkyl, alkenyl, alkynyl, benzyl, and phenethyl; or

A is 

wherein Y^2 is selected from the group consisting of alkyl; cycloalkyl; bicycloalkyl; aryl; monocyclic heterocycles; alkyl optionally substituted with aryl which can also be optionally substituted with one or more substitutent selected from halo, haloalkyl, alkyl, nitro, hydroxy, alkoxy, aryloxy, aryl, or fused aryl; aryl optionally substituted with one or more substituent selected from halo, haloalkyl, hydroxy, alkoxy, aryloxy, aryl, fused aryl, nitro, methylenedioxy, ethylenedioxy, or alkyl; alkylnyl; alkenyl; $-S-R^9$ and $-O-R^9-$ wherein R^9 is selected from the group consisting of H; alkyl; aralkyl; aryl; alkenyl; and alkynyl; or R^9 taken together with R^7 forms a 4-12 membered mononitrogen and monosulfur or monooxygen containing heterocyclic ring optionally substituted with lower alkyl, hydroxy, keto, phenyl, carboxyl or carboxyl ester, and fused phenyl or R^9 taken together with R^7 us thiazole, oxazole, benzoxazole, or benzothiazole; and

R^5 and R^7 are as defined above; or

Y^2 (when Y^2 is carbon) taken together with R^7 forms a 4-12 membered mononitrogen or dinitrogen containing ring optionally substituted with alkyl, aryl, keto or hydroxy; or

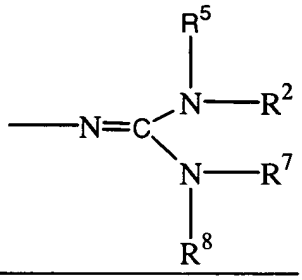
A is 

Where R^2 and R^7 taken together form a 5-8 membered dinitrogen containing heterocycle optionally substituted with one or more substituent selected from the

group consisting of lower alkyl, hydroxy, alkoxy, keto, phenyl, or carboxy derivatives; and R^8 is selected from the group consisting of alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkylcarbonyl, haloalkoxycarbonyl, alkylthiocarbonyl, arylthiocarbonyl, or acyloxymethoxycarbonyl; and

R^5 is defined as above; or

R^2 and R^7 taken together form a imidazole or pyrimidone; or

A is 

where R^2 and R^7 taken together form a 5-8 membered dinitrogen containing heterocycle optionally substituted with hydroxy, keto, phenyl, or alkyl; and

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R^8 and R^5 are both selected for the group consisting of alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkylcarbonyl, haloalkoxycarbonyl, alkylthiocarbonyl, arylthiocarbonyl and acyloxymethoxycarbonyl;

Z^1 is one or more substitutent selected from the group consisting of H; alkyl; hydroxy; alkoxy; aryloxy; halogen; haloalkyl; haloalkoxy; nitro; amino; aminoalkyl; alkylamino; acylamino; dialkylamino; cyano; alkylthio; alkylsulfonyl; carboxyl derivatives; trialoacetamide; acetamide; acyl; aryl; fused aryl; cycloalkyl; thio; monocyclic heterocycles; fused monocyclic heterocycles; and A, wherein A is defined above;

V is selected from the group consisting of –N-(R^6)- wherein R^6 is selected from the group consisting of H; lower alkyl; cycloalkyl; aralkyl; aryl; and monocyclic heterocycles; or R^6 taken together with Y, forms a 4-12 membered mononitrogen containing ring;

Y, Y^3, Z and Z^3 are independently selected from the group consisting of hydrogen; alkyl; aryl; and cycloalkyl; or Y and Z taken together form a cycloalkyl; or Y^3 and Z^3 taken together form a cycloalkyl;

N is an integer 1, 2, or 3;

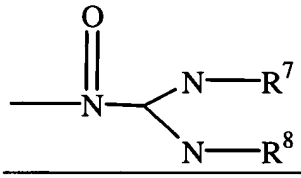
t is an integer 0, 1, or 2;

p is an integer 0, 1, 2, or 3;

R is X—R^3 wherein X is selected from the group consisting of O, S and NR^4, wherein R^3 and R^4 are independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; haloalkyl; aryl; arylalkyl; sugars; steroids; polyalkylethers; alkylamido; alkyl N,N-dialkylamido; pivaloyloxymethyl; and in the case of the free acid, all pharmaceutically acceptable salts thereof;

R^1 is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, carboxyl derivatives; haloalkyl; cycloalkyl; moncyclic heterocycles; monocyclic heterocycles optionally substituted with one or more substituent selected from the group consisting of alkyl, halogen, haloalkyl, cyano, hydroxy, aryl, fused aryl, nitro, alkoxy, aryloxy, alkylsulfonyl, arylsulfonyl, sulfonamide, thio, alkylthio, carboxyl derivatives, amino, amido; alkyl optionally substituted with one or more of halo, haloalkyl, hydroxy, alkoxy, aryloxy, thio, alkylthio, alkynyl, alkenyl, alkyl, arylthio, alkylsulfoxide, alkylsulfonyl, arylsulfoxide, arylsulfonyl, cyano, nitro, amino, alkylamino, dialkylamino, alkylsulfonamide, arylsulfonamide, acylamide, carboxyl derivatives, sulfonamide, sulfonic acid, phosphonic acid

derivatives, phosphinic acid derivatives, aryl, arylthio, arylsulfoxide, or arylsulfone all optionally substituted on the aryl ring with halo, alkyl, haloalkyl, cyano, nitro, hydroxy, carboxyl derivatives, alkoxy, aryloxy, amion, alkylamino, dialkylamino, amido, aryl, fused aryl, moncyclic heterocycles; and fused moncyclic heterocycles, moncyclic heterocyclicthio, moncyclic heterocyclicsulfoxide, and moncyclic heterocyclic sulfone, which can be optionally substituted with halo, haloalkyl, nitro, hydroxy, alkoxy fused aryl, or alkyl;alkylcarbonyl, haloalkylcarbonyl, and arylcarbonyl;
aryl optionally substituted in one or more positions with halo, haloalkyl, alkyl, alkoxy, aryloxy, methylenedioxy, ethylenedioxy, alkylthio, haloalkylthio, thio, hydroxy, cyano, nitro, acyloxy, carboxyl derivatives, carboxyalkoxy; amido, acylamino, amino, alkylamino, dialkylamino, trifluoroalkoxy, trifluoromethylsulfonyl, alkylsulfonyl, sulfonic acid, sulfonamide, aryl, fused aryl, moncyclic heterocycles and fused heterocycles; and



wherein R^7 and R^8 are defined as above and provided that taken together with the nitrogen, R^7 and R^8 comprise an amino acid; and
R^{11} is selected from the group consisting of H, alkyl, aralkyl, alkenyl, alkylnyl, haloalkyl or haloalkylnyl or R^{11} taken together with Y forms a 4-12 membered mononitrogen containing ring.

Claim 14 (Original) A method according to Claim 13 wherein the condition treated is tumor metastasis.

Claim 15 (Original) A method according to Claim 13 wherein the condition treated is solid tumor growth.

Claim 16 (Original) A method according to Claim 13 wherein the condition treated is angiogenesis.

Claim 17 (Original) A method according to Claim 13 wherein the condition treated is osteoporosis.

Claim 18 (Original) A method according to Claim 13 wherein the condition treated is humoral hypercalcemia of malignancy.

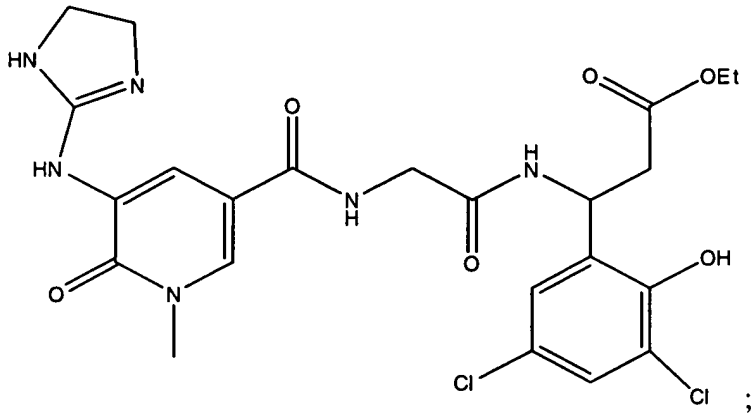
Claim 19 (Original) A method according to Claim 13 wherein the condition treated is smooth muscle cell migration.

Claim 20 (Original) A method according to Claim 13 wherein restenosis is inhibited.

Claim 21 (Original) A method according to Claim 13 wherein the condition treated is rheumatoid arthritis.

Claim 22 (Original) A method according to Claim 13 wherein the condition treated is macular degeneration.

Claim 23 (New) A method for treating conditions mediated by the $\alpha_v\beta_3$ integrin in a mammal in need of such treatment comprising administering a therapeutically effective $\alpha_v\beta_3$ inhibiting amount of a compound selected from the group consisting of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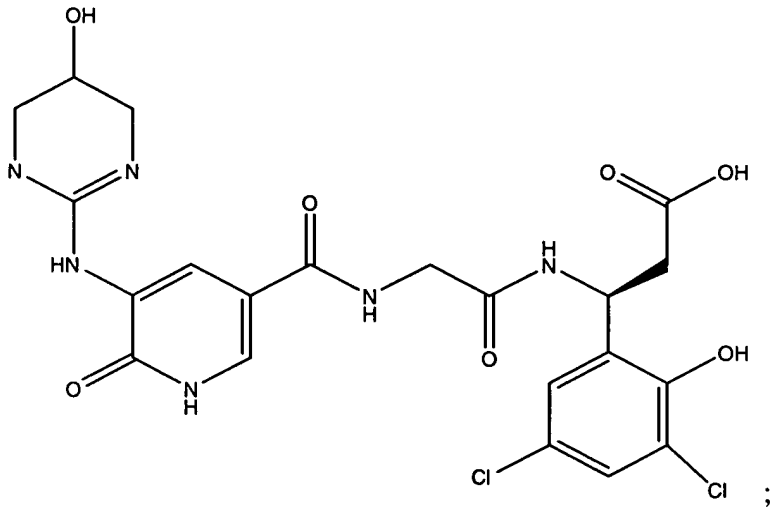
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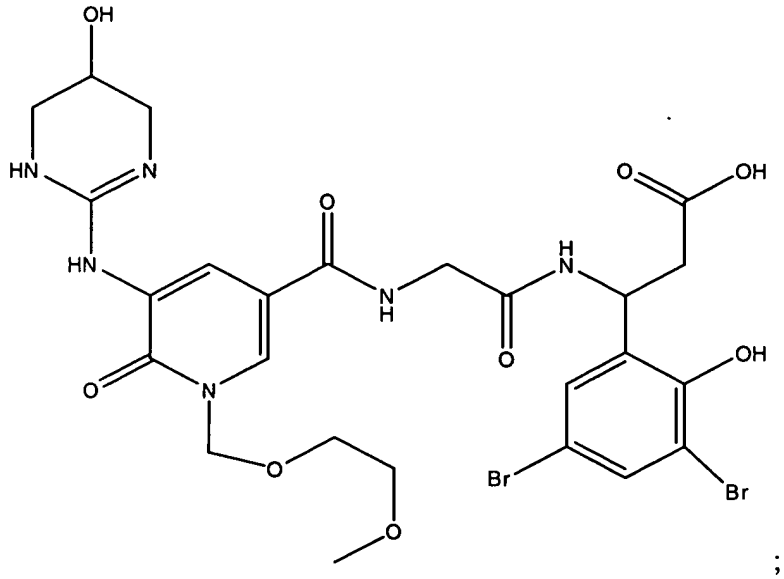
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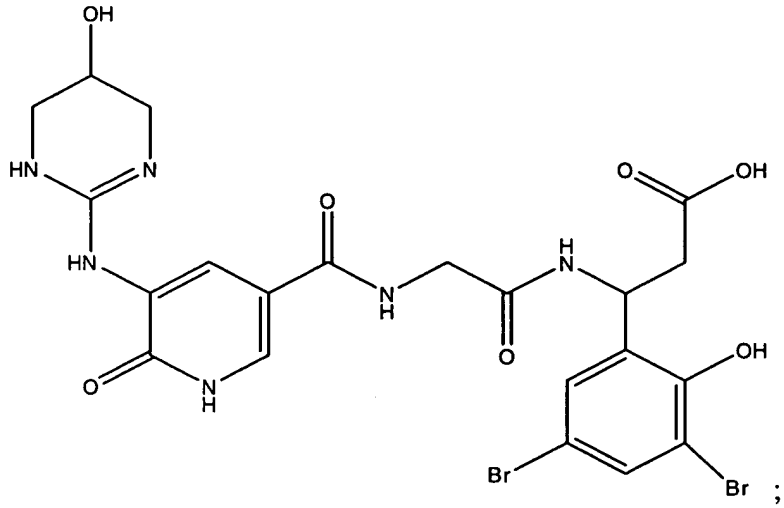
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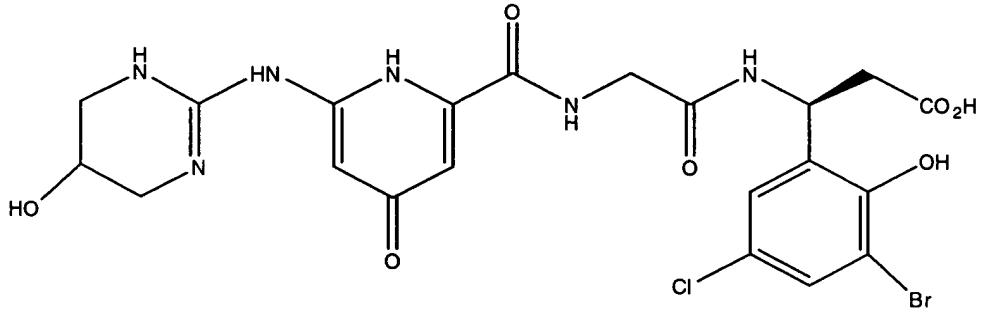
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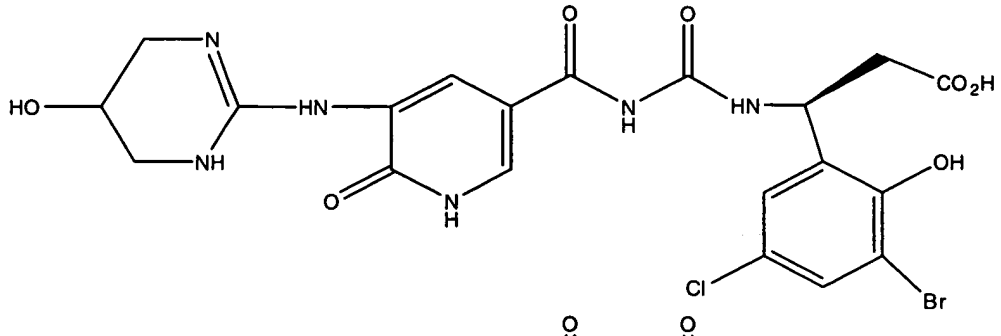

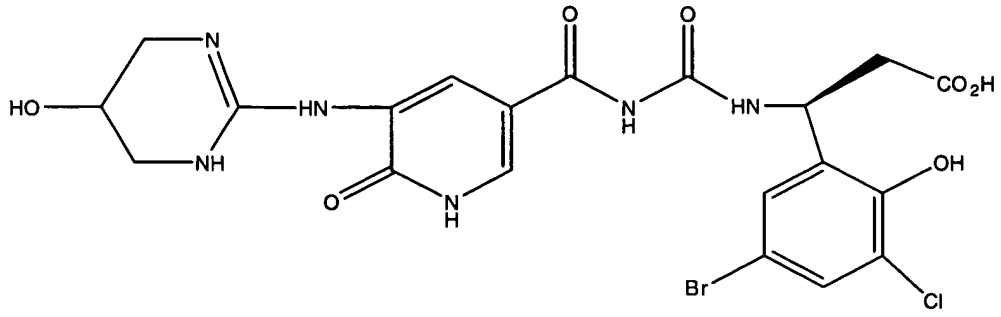

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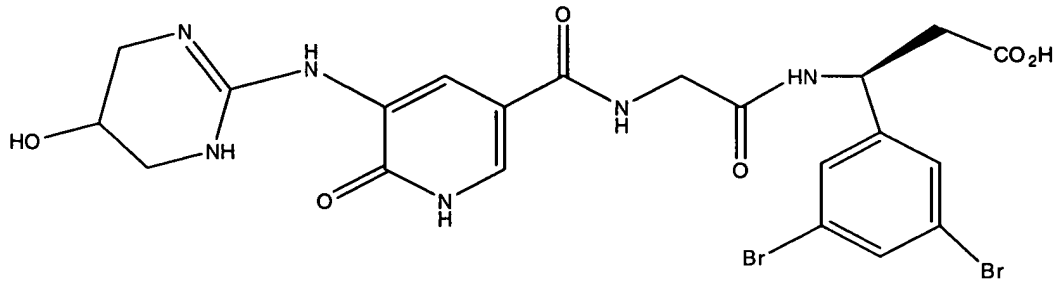

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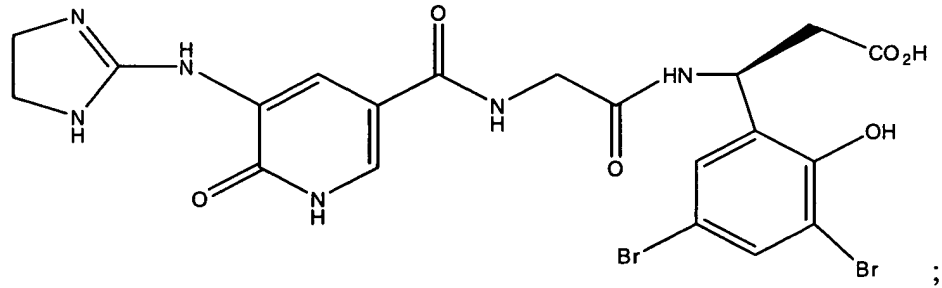

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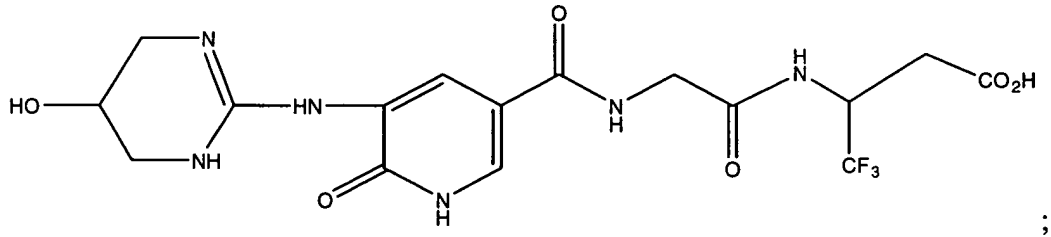

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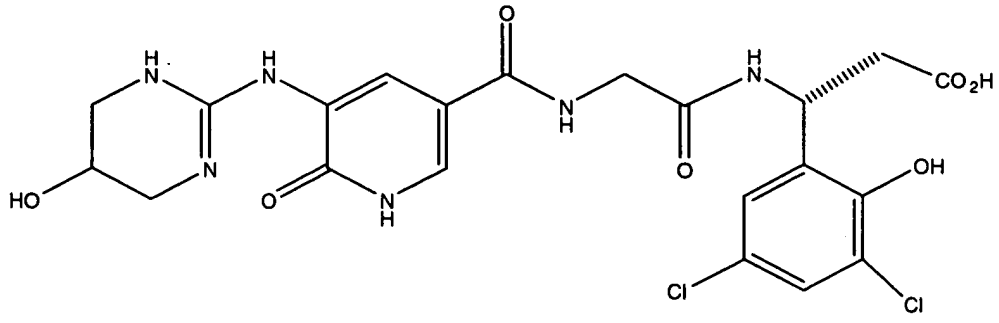
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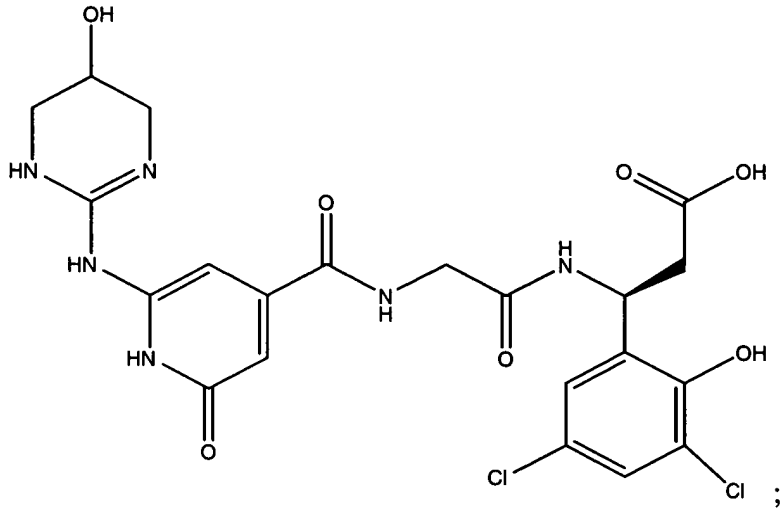
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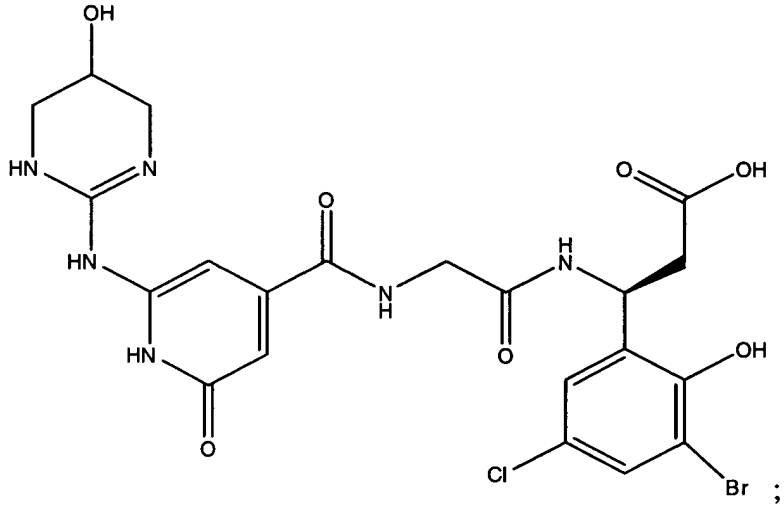
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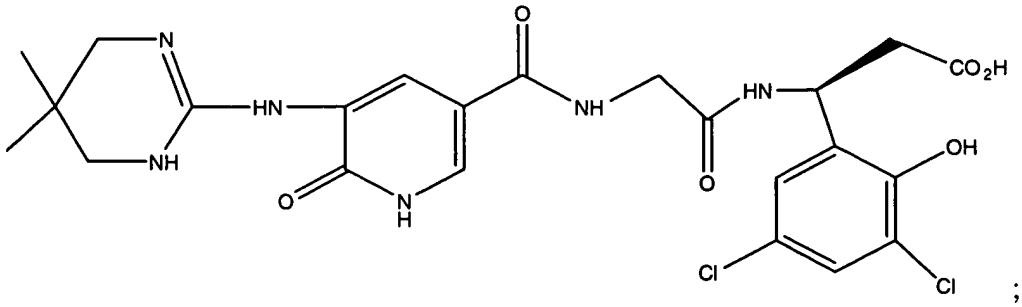

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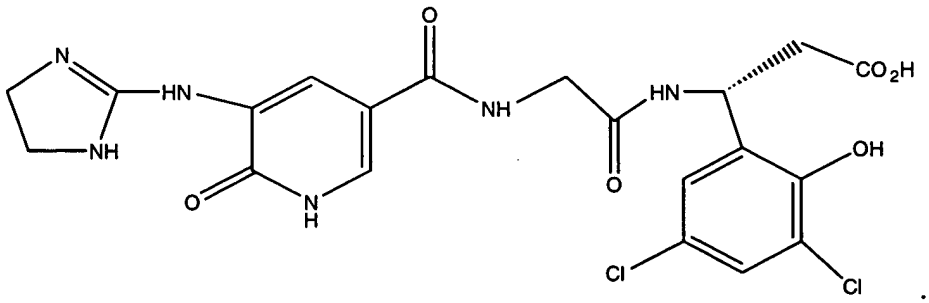

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Claim 24 (New) The method of Claim 23 wherein the condition treated is selected from the group consisting of tumor metastasis, solid tumor growth, angiogenesis, osteoporosis, humoral hypercalcemia of malignancy, smooth muscle cell migration, restenosis, rheumatoid arthritis, and macular degeneration.